

(FILE 'HOME' ENTERED AT 18:17:14 ON 15 JAN 2004)

FILE 'MEDLINE, CANCERLIT, BIOTECHDS, EMBASE, BIOSIS, CAPLUS'  
ENTERED AT

18:17:36 ON 15 JAN 2004

L1 7559 S EBNA OR EBNA-1 OR EBNA-2  
L2 559515 S PROMOTER OR ENHANCER  
L3 1001 S L1 AND L2  
L4 8277502 S INDUC? OR ACTIVA?  
L5 569 S L4 AND L3  
L6 93 S PAPILLOMA VIRUS ANTIGEN  
L7 5 S L6 AND L2  
L8 5 DUP REM L7 (0 DUPLICATES REMOVED)  
L9 116488 S ADENOVIR?  
L10 24 S L9 AND L5  
L11 11 DUP REM L10 (13 DUPLICATES REMOVED)

L11 ANSWER 10 OF 11 MEDLINE on STN DUPLICATE 3  
AN 95133150 MEDLINE  
DN 95133150 PubMed ID: 7831773  
TI Characterization of the Epstein-Barr virus Fp promoter.  
AU Nonkwelo C; Henson E B; Sample J  
CS Department of Virology and Molecular Biology, St. Jude Children's Research  
Hospital, Memphis, Tennessee 38105.  
NC CA-21765 (NCI)  
CA-56639 (NCI)  
SO VIROLOGY, (1995 Jan 10) 206 (1) 183-95.  
Journal code: 0110674. ISSN: 0042-6822.  
CY United States  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals  
EM 199502  
ED Entered STN: 19950307  
Last Updated on STN: 19950307  
Entered Medline: 19950217  
AB Expression of the Epstein-Barr virus nuclear antigen-1 (EBNA-1) protein is mediated by the virus Fp promoter in Burkitt lymphoma and nasopharyngeal carcinoma. This promoter is silent in latently infected B lymphoblastoid and most Burkitt lymphoma-derived cell lines in vitro, which utilize separate promoters approximately 50 kb upstream of Fp to express EBNA proteins. Fp-mediated activation of EBNA-1 expression is also activated upon induction of the virus replication cycle. We previously demonstrated that activation of Fp in Burkitt cells requires cis-regulatory elements downstream of the

site of transcription initiation. We have now mapped two positive regulatory elements within the Fp promoter. One element contains two potential binding sites for the cellular transcription factor LBP-1 between +138 and +150. A second regulatory element was mapped between +177 and +192 and can be specifically bound in vitro by protein from nuclear extracts of Burkitt cells. Although this element overlaps two partial E2F binding sites and Fp reporter plasmids could be activated in trans by the adenovirus E1A protein in cotransfection experiments, mutational analysis and DNA binding studies suggest that these are unlikely to be functional E2F response elements within Fp. We also demonstrate that Fp-directed transcription initiates at multiple sites within both the genome and the Fp reporter plasmids. However, the principal site of transcription initiation within the genome is not utilized within reporter plasmids, in which the majority of transcripts initiate at multiple sites between +150 and +200. This finding suggests that additional elements may be necessary for Fp to function normally in these assays or that the context of Fp within the viral genome is critical to its regulation.

L11 ANSWER 11 OF 11 MEDLINE on STN DUPLICATE 4

AN 92015480 MEDLINE

DN 92015480 PubMed ID: 1656076

TI An Epstein-Barr virus nuclear protein 2 domain essential for transformation is a direct transcriptional activator.

AU Cohen J I; Kieff E

CS Medical Virology Section, National Institutes of Health, Bethesda, Maryland 20892.

NC CA47006 (NCI)

SO JOURNAL OF VIROLOGY, (1991 Nov) 65 (11) 5880-5.

Journal code: 0113724. ISSN: 0022-538X.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199111

ED Entered STN: 19920124

Last Updated on STN: 19980206

Entered Medline: 19911114

AB Epstein-Barr virus nuclear protein 2 (EBNA-2)

increases mRNA levels of specific viral and cellular genes through direct or indirect effects on upstream regulatory elements. The EBNA-2 domains essential for these effects have been partially defined and correlate with domains important for B-cell growth transformation. To determine whether EBNA-2 has a direct transcriptional activating domain, gene fusions between the DNA-binding domain of GAL4 and EBNA-2 were tested in CHO and B-lymphoma

cells for the ability to activate transcription from target plasmids containing GAL4 recognition sites upstream of an adenovirus or murine mammary tumor virus promoter. In B-lymphoma cells, a 37-amino-acid EBNA-2 domain previously identified to be essential for transformation was nearly as strong a transcriptional activator as the activating domain of herpes simplex virus trans-inducing factor VP16. A quadradecapeptide had about 25% of the activating activity of the longer peptide. This first evidence that EBNA-2 directly activates transcription should facilitate the identification of nuclear factors with which EBNA-2 interacts in transactivation and transformation.

L11 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1999:393034 CAPLUS

DN 131:40554

TI Oncogene or virus induced multistep expression systems for gene therapy

IN Muller, Rolf; Sedlacek, Hans-Harald

PA Hoechst Marion Roussel Deutschland GmbH, Germany

SO Eur. Pat. Appl., 44 pp.

CODEN: EPXXDW

DT Patent

LA German

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 922768	A2	19990616	EP 1998-121471	19981111
EP 922768	A3	20000105		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
DE 19751587	A1	19990729	DE 1997-19751587	19971121
CA 2251257	AA	19990521	CA 1998-2251257	19981119
AU 9893256	A1	19990610	AU 1998-93256	19981119
AU 745614	B2	20020328		
CN 1221033	A	19990630	CN 1998-122537	19981120
BR 9804720	A	20000328	BR 1998-4720	19981120
US 6465246	B1	20021015	US 1998-196099	19981120
JP 2000106886	A2	20000418	JP 1998-333200	19981124
PRAI	DE	1997-19751587	A	19971121

AB The invention concerns a DNA construct for the expression of an effector gene contg. promoter I (component a) that regulates the expression of the transcription factor gene (component b); promoter II (component c) that is specifically bound by the product of the transcription factor gene and that regulates the expression of the effector gene (component d); all components are part of the same

DNA construct; the activity of the gene product of the transcription factor gene is dependent on one or more cellular regulatory protein(s), that bind specifically to the gene product and influence its activity. The invention also concerns cells hosting the construct and the application for gene therapy and prodn. of gene therapeutics. Effector genes are coding for pharmacol. active substances, pharmacocons, enzymes or their precursors, or fusion proteins with signal proteins; and are used for therapy or prophylaxis. In one of the versions the component b consists of the b1 activation domain, the b2 regulatory protein binding sequence, and the b3 DNA-binding domain for a transcription factor. The b2 sequence is a viral or bacterial binding protein sequence; this ensures that in healthy cells the function of the transcription factor gene is inhibited; regulatory proteins that are produced in infected cells bind to the sequence; thus the transcription factor becomes activated. In a specific version b2 represents an antibody or antibody fragment with VH or VL binding sequences for a regulatory protein; humanized murine antibodies, recombinant antibody fragments produced in hybridoma cells, or isolates from libraries are used. DNA expressing the antibody fragments are ligated to b1 and b3 components. Examples of activation domains (component b1) are: cDNA for the acidic transactivation domain of HSV1-VP16, activation domain of Oct-2, SP1, NFY etc. Examples of DNA-binding domains (component b2) are: cDNA for the DNA-binding domains of Gal4 protein, LEXA protein, lac-repressor protein, etc. In another version the construct consist of promoter I (component a'), the repressor (component b'); the activation sequence (component c1) induced by b'; the DNA binding sequence for the repressor protein (component c2). The promoter I (component a') consists of a DNA-binding sequence for a regulatory protein (component a1), and a basal promoter (component a2). Examples for component a1 are: the DNA binding sequences of p53 protein, Wt-1 protein, NF-Kappa B protein, E2f/DP1 complex, and Myc/Max protein. Examples for component a2 are: the basal promoter of SV40, c-fos, U2 sn RNA-promoter, HSV TK promoter. Activation sequences are (component a or component c1): non-constitutive activation promoters, e.g. promoters of RNA polymerase II and III, CMV promoter and enhancer, SV40 promoter; viral promoters and activation sequences, e.g. HBV, HCV, HIV, etc.; promoters with metabolic activation, e.g. hypoxia induced enhancer; promoters that are activated cell cycle-specific, e.g. promoters of the genes cdc25c, Cyclin A etc.; tetracyclin induced promoters; cell specific promoters, e.g. promoters and activation sequences of endothelial cells, or of contiguous cells, smooth muscle cells, glial cells etc. The effector genes are for tumor therapy, with the following target cells: endothelium, stroma cells, muscle cells, tumor cells, leukemia cells. The effector

genes include cell specific promoters, inhibitors for cell proliferation, blood activation factor inducing genes, angiogenesis inhibitors, cytostatics, cytotoxics, cytokines, growth factors, etc. also in form of fusion proteins.

L11 ANSWER 8 OF 11 MEDLINE on STN DUPLICATE 2  
AN 97404671 MEDLINE  
DN 97404671 PubMed ID: 9261383  
TI Epstein-Barr virus nuclear protein LP stimulates EBNA-2  
acidic domain-mediated transcriptional activation.  
AU Harada S; Kieff E  
CS Channing Laboratory, Department of Medicine, Brigham and Women's Hospital,  
Boston, Massachusetts, USA.  
NC CA47006 (NCI)  
SO JOURNAL OF VIROLOGY, (1997 Sep) 71 (9) 6611-8.  
Journal code: 0113724. ISSN: 0022-538X.  
CY United States  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals  
EM 199709  
ED Entered STN: 19970926  
Last Updated on STN: 19970926  
Entered Medline: 19970917  
AB Epstein-Barr virus (EBV) nuclear proteins EBNA-LP and  
EBNA-2 are the first two proteins expressed in latent  
infection of primary B lymphocytes. EBNA-2 is  
essential for lymphocyte transformation, and EBNA-LP is at least  
critical. While EBNA-2 activates specific  
viral and cellular promoters, EBNA-LP's role has been obscure.  
We now show that EBNA-LP stimulates EBNA-2  
activation of the LMP1 promoter and of the LMP1/LMP2B  
bidirectional transcriptional regulatory element. EBNA-LP alone  
has only a negative effect. EBNA-LP also stimulates  
EBNA-2 activation of a multimerized regulatory  
element from the BamC EBNA promoter. Since both viral  
regulatory elements can bind the EBNA-2-associated  
cell protein RBPJ kappa, consensus RBPJ kappa binding sites were  
positioned upstream of the herpes simplex virus type 1 thymidine kinase  
promoter and were found to be sufficient for EBNA-LP and  
EBNA-2 coactivation. EBNA-LP strongly  
stimulated activation of an adenovirus E1b  
promoter with upstream Gal4 binding sites by a Gal4 DNA binding  
domain/ EBNA-2 acidic domain fusion protein,  
indicating that EBNA-LP coactivation requires only the

EBNA-2 acidic domain to be localized near a promoter. The EBNA-LP stimulatory activity resides in the amino-terminal 66-amino-acid repeat domain. The carboxyl-terminal unique 45 amino acids appear to regulate EBNA-LP's effects. The first 11 amino acids of the 45 have a strong negative effect, while the last 10 are critical for the ability of the last 34 to relieve the negative effect. These results indicate that EBNA-LP's critical role in EBV-mediated cell growth transformation is in stimulating (and probably regulating) EBNA-2-mediated transcriptional activation.